PROLONGED FASTING IN DIABETES.[1]

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Partial pancreatectomy, with preservation of the pancreatic duct so as to avoid atrophy of the remnant, gives a more satisfactory reproduction of clinical diabetes than is afforded by von Mering and Minkowski's total pancreatectomy or Sandmeyer's method of slow pancreatic atrophy. Simple lowering of the sugar tolerance without diabetes, or diabetes varying in intensity from the mildest to the very severe, can thus be produced at will. As previously pointed out,[2] animals thus prepared constitute valuable test-objects and afford favorable opportunities for research concerning diabetic therapy. In the milder types the measures ordinarily used in human diabetes, namely, restriction of carbohydrate or protein and brief fasting, if necessary, suffice to keep the animals sugar-free and in good condition indefinitely. But in a more severe type these measures do not suffice and the animal quickly passes into a hopeless condition if more radical treatment is delayed. In this type the initial fast must sometimes be measured in weeks rather than in days. The subsequent diet must be such as to keep the animal at a low level of weight and metabolism. Certain influences which increase either weight or metabolism tend to bring back glycosuria in these animals as in human patients. If glycosuria persists in any animal the result is a downward sequence of lowered tolerance, emaciation, weakness, cachexia, and death, with parallel degenerative changes in the islands of Langerhans. If glycosuria is prevented, the animals may remain lively and strong though thin; they may improve somewhat with time, and the islands seem to be spared. This evidence supports the hypothesis that one set of influences overtax and injure the internal function of the pancreas, and the opposite set of influences protect and rest the internal function of the pancreas.

The treatment of diabetes at the Rockefeller Hospital has been based upon these animal experiments. The patients admitted have been forty-four, chosen as the most severe out of a considerable number of applicants, and representing a sufficient variety as respects age, social condition, and other factors. Certain points may here be mentioned concerning (1) the initial fast and (2) the subsequent diet.

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[1] Read at the meeting of the Association of American Physicians, Washington, D. C., May, 1915.

[2] Allen, F. M., Studies Concerning Glycosuria and Diabetes, Harvard University Press, Cambridge, Massachusetts.

Fasting has been employed by writers from Naunyn to Guelpa. The same writers describe a numerous class of diabetics who are not made sugar-free, but go on with glycosuria and acidosis and die in coma. Other patients are made sugar-free only after months of strict dietary treatment, including occasional single or repeated fast-days. Present experience indicates that the glycosuria in cases of even the severest type of diabetes may with advantage be cleared up by one initial fast. The necessary duration may sometimes be as long as eight or ten days. In one case of maximum severity in a youth, aged seventeen years, the changes accompanying fasting were studied by Dr. Eugene Du Bois in the respiration calorimeter. He found that at the outset the total metabolism was about 8 per cent. above normal and the patient was excreting all or nearly all of the sugar formed from protein and burning practically no sugar at all. In a nine days fast the glycosuria ceased, the total metabolism fell to about 20 per cent. below normal, and the respiratory quotient showed that the sugar formed from protein was being burned. It will be remembered that respiratory quotients in the most severe cases during the "oat cure" do not show increased combustion of carbohydrate. The above metabolic observations are new and constitute important evidence for the functional element in the etiology of human diabetes, since they show to what extent recovery can take place within a few days when the most complete possible rest is given the weakened metabolic function.

Severe acidosis, which is known to be diminished by the shorter fasts previously employed, is still more reduced by the more prolonged fasting. Dangerously weak and emaciated patients have borne the fasting with apparent benefit, giving the impression that they had been suffering more from intoxication than from lack of nutrition. Alcohol is valuable during fasting as a food which does not produce glycosuria, though its use is not essential. Broadly speaking, freedom from glycosuria seems attainable in all cases of uncomplicated human diabetes before there is danger of death from starvation. In a few cases seen personally or described by others, death from some severe complication has occurred before the urine became sugar-free. In such cases to date the complication has been a severe infection, or some condition strongly tending to increase metabolism or produce nervous or circulatory disturbance. The fasting has not appeared harmful even in these few cases where it has not been successful. One case of incipient gangrene and one dangerous carbuncle cleared up rapidly under fasting, and threatening complications of infectious or any other character are considered an indication for the radical treatment as described. No contraindication has been met, unless it be the appearance of nausea, vomiting, and prostration while fasting. One woman died in such an attack; but there were attacks of this character in her previous history, and it is not positive that either the attack or the death was due to the fasting. One man began to vomit and feel unwell on the seventh day of fasting. He was fed and the symptoms immediately passed off. After two weeks of restricted diet a second fast easily cleared up the glycosuria. This simple precaution apparently prevents danger even in this rare type of cases, and in other cases there has never been any sign of danger or harm.

Though the initial fast, to clear up glycosuria and other symptoms, is generally a very simple matter, the subsequent diet, to maintain this condition, is sometimes difficult. It is unquestionably true, in accord with Joslin's[3] warning, that when glycosuria is abolished and strength diminished by long fasting, and then glycosuria and acidosis allowed to return through improper diet, the last state of that man may be worse than the first. Herein may be found the causes of failure in past attempts of this sort. After the fasting patient has been completely sugar-free for one or two days, feeding is begun as outlined in former papers,[4] and the tolerance of the patient for carbohydrate, protein, and fat is determined. Just as fasting is continued not for any limited number of days, but as long as necessary for sugar-freedom, so also the diet is governed not by any theoretical standard of protein or calories, but by the amount of each food that can be given in each individual case while keeping the urine clear. Under this program even weak and emaciated patients have been subjected to under-nutrition in both protein and calories for weeks or months continuously, with ultimate benefit. Any trace of glycosuria is the signal for a fast-day with subsequent modification of diet, and routine fast-days are often used as frequently as once a week even in absence of glycosuria. While individual details must be reserved to a later publication, two principles in the management of severe cases may be mentioned, namely, the benefit of keeping the patient permanently below weight, and the advisability of restricting the quantity of fat in the diet.

A slight temporary reduction of weight was practiced in some cases by Naunyn, whose example has been widely followed. This was not carried to the point of abolishing glycosuria and acidosis in the severest cases; and generally the attempt has been to maintain these patients at the highest possible level of weight and nutrition, with the idea of helping them to withstand a wasting disease. The present idea is the opposite to this, namely, that the reduction of weight is in itself beneficial to the diabetic condition and serves to spare the weakened function and increase tolerance. This measure, like the others, is carried to any point that may be necessary in any particular instance. Sometimes a slight reduction of weight suffices even for a severe case. Again, a well-nourished patient, easily kept free from glycosuria, was reduced by twenty kilograms merely because of a slight stubborn ketonuria and a persistently high blood-sugar. Most patients are able to regain weight to a greater or less extent, but few severe ones are able to return fully to normal weight. Any increase that is possible without return of symptoms is permitted. Any gain that brings back glycosuria or ketonuria is checked. The experience in human patients thus far runs parallel to that in the animal experiments upon which this suggestion was founded.

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[3] Discussion of paper at meeting of Suffolk County Medical Society in connection with Boston Medical Library, December 2, 1914.

[4] Allen, F. M., Jour. Amer. Med. Assoc., September 12, 1914; Boston Med. and Surg. Jour., February 18, 1915.

In the treatment of diabetes heretofore, fat has been freely given and even forced upon the patient. It has been restricted only in certain cases with high acidosis and danger of coma. The doctrine has been that fat does not affect diabetic glycosuria except in very rare "fat-sensitive" patients; also, that the diabetic must receive the number of calories required by his metabolism, plus the number of calories lost as sugar and acetone bodies in the urine, and fat has been considered the best food for crowding in these calories. Anyone can readily convince himself that, in a suitably severe diabetic who is symptom-free for days or weeks on a fixed diet, the addition of some quantitiy of butter or olive oil to the diet will bring back the glycosuria, ketonuria, and other symptoms immediately or within a short time. The feeding of fat alone does not cause glycosuria, and there is no proof that the sugar is formed from the fat; more probably the sugar excretion results from the stimulating effect of fat upon metabolism. The overtaxing of the patient's metabolism by giving fat beyond the limit of tolerance may be an additional explanation of the failure to keep certain patients free from glycosuria and ketonuria under former methods of treatment.

Concerning any proposed treatment, inquiry is proper whether it is new and whether its results are superior to those of the old methods. The following statements can be made regarding these points.

The principle tentatively suggested that increase of weight or metabolism increases strain upon the internal pancreatic function and reduction of weight or metabolism reduces strain upon the internal pancreatic function, is new, and if it proves valid will be a useful general guide in treatment. The animal experiments likewise are entirely new. The general policy of insisting upon prompt and lasting freedom from glycosuria and acidosis in all cases of diabetes, even the severest, is a new one. In addition, the main features wherein the proposed treatment differs from the previously established methods may be summarized under the following five headings. The first two represent differences merely of degree, in that the proposed treatment is more radical than the old; namely, first, an initial fast sufficient to clear up glycosuria in any case and then one or two days longer; second, a subsequent diet such as to keep glycosuria and acidosis permanently absent, with as many interspersed fast-days as necessary for this purpose. The third and fourth features represent differences not in degree but in kind, and are diametrically opposed to the prevalent teachings; that is, the third opposes the idea that the diabetic should be kept at the highest possible level of weight and strength, and that gain in weight is synonymous with improvement; and it substitutes for this the plan of keeping most severe diabetics intentionally and permanently at a sufficiently low level of weight and metabolism, in the belief that return of symptoms and downward progress is thus prevented. The fourth feature stands opposed to the doctrines that fat feeding does not appreciably influence diabetic glycosuria, and that calories lost in the urine should be replaced by additional calories in the diet, preferably in the form of fat. It opposes to these the observation that addition of fat to a fixed diet suffices to bring back both glycosuria and ketonuria in most severe diabetics, and the principle that the patient's tolerance for fat and calories should be followed in the same way as the tolerance for carbohydrate and protein. The fifth feature consists merely of routine or incidental matters, which are not without practical importance. Among these may be mentioned (1) the diet such as not to overtax tolerance and yet satisfy the patient sufficiently that he will follow it continuously at home; (2) the absence of any specific craving for carbohydrate such as diabetics are supposed to manifest, and the contradiction of the prevalent idea that most severe diabetics cannot be trusted; (3) the avoidance of the need of alkali for more than a few days, and therewith relief from disturbances due either to acidosis on the one hand or to prolonged large doses of soda on the other; (4) the principle of clearing up the urine quickly and devoting the greater part of the stay in hospital to educating the patient, rather than devoting the greater part of the stay in hospital to clearing up the urine and dismissing the patient shortly thereafter; (5) instruction of the patient in the simple means of controlling his own condition, through his diet, his body weight, and the daily testing of his own urine with Benedict's solution.

The immediate results as observed up to the present have appeared uniformly beneficial. Reports from a number of clinicians experienced in the older methods of treating diabetes agree that these results under the new method are more favorable. Also the relative simplicity of the proposed method, and the fact that it stops glycosuria without running any risk of acidosis, makes it available for a large body of general practitioners who have heretofore not felt safe in withdrawing carbohydrate or attempting to stop glycosuria in cases with any marked ketonuria. Patients also generally accept radical treatment with quick decisive results more readily than the weeks or months of privation heretofore used in stopping glycosuria, and the quick relief from polyphagia, polydipsia, and other symptoms aids further in securing their coöperation. For these reasons it is believed that the innovations described are of some real value. As respects the remote results and the influence on the ultimate prognosis of severe diabetes, longer experience must decide. A question is here involved whether diabetes is an inherently progressive disease or whether it is the simple weakness of a metabolic function. If it is the former, patients must ultimately go down hill and die, though not in diabetic coma, and the benefit will consist only in lengthening their lives and keeping them more comfortable. If it is the latter, downward progress may be indefinitely prevented by avoiding overstrain of the weak function, just as in animals. Among the patients treated thus far, during a variable number of months in the hospital and at home, spontaneous downward progress has not yet been observed. Whatever the ultimate outcome, two conclusions seem justified by present knowledge: (1) that this treatment removes glycosuria and acidosis more quickly and surely than has been the practice heretofore, and (2) that patients do better when glycosuria and acidosis are removed than when they are allowed to continue.

PRESENT-DAY TREATMENT AND PROGNOSIS IN DIABETES.

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It is no exaggeration to say that the advance in the actual treatment of diabetes mellitus during the twelve months just passed has been greater than in any year since Rollo's time, and it should be emphasized that this improvement in treatment comes not by chance, but as a result of patient scientific experimentation, which has been based upon the work of the foremost investigators in both laboratory and clinic. It follows experiments upon animals, and is an answer to those critics who have claimed that animal experimentation in diabetes had failed to justify itself. At the same time better and simpler technical methods for the study of the blood, urine and respiratory exchange, as well as new knowledge of the metabolism of diabetes, have contributed a share to this improvement. The truthfulness of the foregoing is easily shown. One year ago physicians were generally afraid to teach their patients to test their urines for sugar; today the physician feels himself